Retroperitoneal Germ Cell Tumor Treated by PVeBV Chemotherapy: a Case Report

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The extragonadal germ cell tumor are uncommon neoplasms which account for only 1–5% of germ cell tumors, and its prognosis is poor. We report here the use of combination chemotherapy with cisplatin, etoposide, bleomycin, and vinblastine (PVeBV) for the treatment of retroperitoneal germ cell tumor. A 28-year-old male with complaints of abdominal pain and lumbago, without any abnormality in both tests by physical and ultrasonographic examination, showed retroperitoneal tumor by abdominal computed tomography. The serum alpha-fetoprotein and lactate dehydrogenase were elevated. The retroperitoneal tumor was treated surgically. The pathological diagnosis was mixed germ cell tumor. The lung and supraclavicular lymph node metastases disappeared completely after 3 courses of PVeBV chemotherapy with cisplatin (40 mg/m² per day) and etoposide (100 mg/m² per day) for 5 consecutive days, with vinblastine (0.2 mg/kg) on day 1, and bleomycin (30 mg/body) given on days 1, 8, and 15. Granulocyte colony-stimulating factor and serotonin receptor antagonist application were available on acute phase toxic effects. The patient is now alive and well, without recurrence, more than 26 months after the operation.

Key words: extragonadal germ cell tumor – retroperitoneum – PVeBV chemotherapy

INTRODUCTION

The extragonadal germ cell tumors (EGCTs) are uncommon neoplasms which account for only 1–5% of germ cell tumors (1), and most EGCTs arise from the mediastinum or retroperitoneum in young males (2). Approximately 85–90% of non-seminomatous EGCTs have metastases at the time of diagnosis (3). The disease is usually advanced when it becomes symptomatic, and further delay may occur before a correct diagnosis is made. Although cisplatin-based chemotherapy is effective against germ cell tumors testicular in origin, the prognosis of EGCTs seems unfavorable (4). Here we report the use of 3 cycles of combination chemotherapy with cisplatin, etoposide, bleomycin, and vinblastine (PVeBV) for the treatment of a case of EGCT arising from the retroperitoneum.

CASE REPORT

A 28-year-old male was admitted to a local hospital in August 1997, complaining of lower abdominal pain and lumbago which had lasted for one month. He had no significant medical history or other familial history of note. Abdominal computed tomography (CT) scans and ultrasonography (US) showed a retroperitoneal mass extending from the level of the renal hilus to that of the aortic bifurcation. The patient was referred to our hospital for treatment on September 10. A physical examination revealed a mass in the left lower quadrant of the abdomen, but superficial lymph nodes were not palpable and bilateral testes were normal on palpation and US examination. A blood chemistry revealed elevated levels of lactate dehydrogenase (LDH) at 577 IU/l. While the alpha-fetoprotein (AFP) serum levels was 169.3 ng/ml, levels of beta-subunit of human chorionic gonadotropin (beta-hCG), carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) were within normal ranges. Abdominal CT and magnetic resonance imaging (MRI) showed a bulky retroperitoneal mass extending from the level of the renal hilus to that of the aortic bifurcation. The patient was referred to our hospital for treatment on September 10. A physical examination revealed a mass in the left lower quadrant of the abdomen, but superficial lymph nodes were not palpable and bilateral testes were normal on palpation and US examination. A blood chemistry revealed elevated levels of lactate dehydrogenase (LDH) at 577 IU/l. While the alpha-fetoprotein (AFP) serum levels was 169.3 ng/ml, levels of beta-subunit of human chorionic gonadotropin (beta-hCG), carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) were within normal ranges. Abdominal CT and magnetic resonance imaging (MRI) showed a bulky retroperitoneal mass involving psoas muscle and multiple para-aortic lymph nodes swelling (Fig. 1), and CT scans of the chest showed a multiple metastatic nodules, up to 10 mm in diameter, in the lung. The patient’s disease was diagnosed as EGCT of retroperitoneal origin or metastatic adrenal tumor of poorly differentiated adenocarcinoma. Because the abdominal pain and lumbago of the patient have severely developed, the tumor resection and retroperitoneal lymphadenectomy were performed on September 24, for the purpose of pain control, differential diagnosis, and cyto-reduction. The tumor, measuring 9.0 × 6.5 × 5.0 cm in size, consisted of a relatively soft, well demarcated solid mass with...
yellowish-white cut surface. A pathological examination demonstrated a mixed germ cell tumor, in which yolk sac tumor and seminoma contained with the formation of cartilage, with vascular invasion within extensive necrosis (Fig. 2). An enlarged left supraclavicular lymph node was palpated after operation, and serum CA19-9 level was elevated to 105.5 U/ml.

The patient received PVeBV chemotherapy, consisting of cisplatin (40 mg/m² per day) and etoposide (100 mg/m² per day) for 5 consecutive days, with vinblastine (0.2 mg/kg) on day 1, and bleomycin (30 mg/body) given on days 1, 8, and 15. Subsequent cycles of chemotherapy were given 21 days after the preceding cycle. After 3 cycles of chemotherapy, in which granulocyte colony-stimulating factor (G-CSF), platelet transfusion, and serotonin (5-HT₃) receptor antagonist were used, the serum AFP and CA19-9 levels were normalized. The lung and lymph node metastases had completely disappeared. The patient has been observed for 26 months without recurrence (Fig. 3).

**DISCUSSION**

EGCTs are rare and have been the source of much controversy and diagnostic difficulty in terms of determining their site of origin. However, throughout the last decades, there has been general agreement that germ cell tumors existing at extragonadal sites are EGCTs when the testes show no clinical signs of tumor on palpation (5). Occasionally, in patients with presumed EGCTs, a fibrous scar is found in the testis at autopsy (6), or a gonadal primary tumor becomes evident during follow-up (7). Daugaard et al. (8) reported testicular biopsy to have shown carcinoma-in-situ in eight of 15 patients (53%) with clinical EGCT. Therefore, before rendering a diagnosis of EGCT, serial section of the testes was proposed as a requirement. Otherwise, Fuchs et al. (9) reported that testicular biopsy or orchiectomy with step section should not be performed in the diagnosis of EGCTs in the absence of a clearly defined testicular mass on physical examination or by testicular ultrasound. In this case, testicular biopsy was not performed according to the specific criterion of ‘probable germ cell tumors of extragonadal origin’ (10).

AFP and beta-hCG are invaluable tumor marker in the diagnosis and follow-up of non-seminomatosus germ cell tumor, and LDH has also been reported to have prognostic significance (11). As part of the initial evaluation in young patients with undiagnosed abdominal or chest masses, LDH, AFP, and beta-hCG levels should all be measured.
The patient's clinical course with the serial changes of the serum CEA, CA19-9, and LDH levels. PVeBV, chemotherapy with cisplatin, etoposide, bleomycin, and vinblastine; AFP, alpha-fetoprotein; CA19-9, carbohydrate antigen 19-9; LDH, lactate dehydrogenase.

The treatment of young men with disseminated testicular cancer has been revolutionized by combination chemotherapy based primarily on cisplatin, vinblastine, and bleomycin (PVB). Variations of this regimen have been reported to induce complete responses (CR) in approximately 75% of patients with metastatic disease, and surgical debulking of residual tumor after chemotherapy in partial responders has increased the number of patients who are disease-free currently (12). Several studies have concluded that patients with non-seminomatous EGCTs have poorer chances of survival than patients with testicular tumors (2,13). Feun et al. (13) described 3 CR in 19 patients (18.8%) with EGCTs treated with PVB. Garnick et al. (14) reported 5 CR in 15 EGCT patients (33.3%) treated with PVB chemotherapy, and four remained in CR for a median survival time of 40 months. Hainsworth et al. (3) reported 21 CR among 31 advanced EGCT patients (67.7%) treated with PVB chemotherapy, and with or without doxorubicin, but their series included 6 patients with seminoma and specifically excluded patients with yolk sac tumors because of their poorer prognosis. The poor prognostic features of EGCTs reflect either the site of origin, treatment-resistant histologic type, or a high tumor burden.

The PVeBV regimen produced better results than PVB in patients with highly advanced testicular tumors (15), while Blayney et al. (16) concluded that cisplatin dose-escalation achieved severe toxicity, and modifications of the regimen to reduce toxicity without diminishing the efficacy should be considered. They used PVeBV regimen in 5 EGCT patients, and 3 patients died from complications therapy. The dose-limiting factor of combination chemotherapy used against testis tumors is almost always myelosuppression, and G-CSF seems promising in chemotherapy against EGCTs as well as that against testis tumor (17). In this case, G-CSF and 5-HT3 receptor antagonist application and vigorous hydration were available on acute phase toxic effects (myelosuppression, nausea and vomiting, and nephrotoxicity), and enabled 3 courses of the regimen as scheduled and without dose reduction. Long term toxic effects such as peripheral neuropathy and ototoxicity were also tolerable, and quality of life in this case was preserved well.

We have reported here a case of retroperitoneal germ cell tumor in male who was treated effectively by PVeBV chemotherapy. The role of PVeBV chemotherapy in treating EGCTs remains to be established in prospective studies.

References